

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 2

Please amend the subject application as follows:

In the Specification:

Please replace the paragraph on page 22, lines 9-14 with the following amended paragraph:

In the preferred embodiment of this invention, the isolated nucleic sequence is cDNA from human as shown in Figures 47A-47D (SEQ ID NO:1). This human sequence was submitted to GenBank (Los Alamos National Laboratory, Los Alamos, New Mexico) with Accession Number, M99487 and the description as PSM, Homo sapiens, 2653 base-pairs.

Please replace the paragraph on page 12, lines 26-31 with the following amended paragraph:

Figures 31A-31D:

The DNA sequence of the 3 kb XhoI fragment of p683 which includes 500 bp of DNA from the RNA start site was determined Sequence 683XFRVS starts from the 5' distal end of PSM promoter (SEQ ID NO:109).

Please replace the paragraph on page 14, lines 15-24 with the following amended paragraph:

Figure 39:

Intron 1F: Forward Sequence. Intron 1 contains a number of trinucleotide repeats which can be area associated with chromosomal instability in tumor cells. LNCaP cells and primary prostate tissue are identical, however in the

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 3

PC-3 and Du-145 tumors they have substantially altered levels of these trinucleotide repeats which may relate to their lack of expression of PSM (SEQ ID NO:110).

Please replace the paragraph on page 14, lines 26 and 27 with the following amended paragraph:

Figures 40A-40B:

Intron 1R: Reverse Sequence (SEQ ID NO:111)

Please replace the paragraph on page 14, line 29 with the following amended paragraph:

Figure 41:

Intron 2F: Forward Sequence (SEQ ID NO:112)

Please replace the paragraph on page 14, line 31 with the following amended paragraph:

Figure 42

Intron 2R: Reverse Sequence (SEQ ID NO:113)

Please replace the paragraph on page 14, lines 33 and 34 with the following amended paragraph:

Figure 43A-43B:

Intron 3F: Forward Sequence (SEQ ID NO:114)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 4

Please replace the paragraph on page 14, lines 35 and 36 with the following amended paragraph:

Figures 44A-44B:

Intron 3R: Reverse Sequence (SEQ ID NO:115)

Please replace the paragraph on page 14, line 37 to page 15, line 1 with the following amended paragraph:

Figures 45A-45B:

Intron 4F: Forward Sequence (SEQ ID NO:116)

Please replace the paragraph on page 15, lines 2 and 3 with the following amended paragraph:

Figures 46A-46B:

4R: Reverse Sequence (SEQ ID NO:117)

Please replace the paragraph on page 15, lines 6-9 with the following amended paragraph:

Figures 47A-47D:

Sequence of the genomic region upstream of the 5' transcription start site of PSM (SEQ ID NO:118)

Please replace the paragraph on page 17, lines 4-11 with the following amended paragraph:

Figures 58A-58C:

Nucleic acid of PSM genomic DNA is read 5 prime away from the transcription start site: number on the sequences

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 5

indicates nucleotide upstream from the start site.
Therefore, nucleotide #121 is actually -121 using
conventional numbering system (SEQ ID NO:119).

Please replace the paragraph on page 18, lines 24 and 25 with
the following amended paragraph:

Figures 72A-72D:

Intron 1F: Forward Sequence (SEQ ID NO:120)

Please replace the paragraph on page 18, lines 27 and 28 with
the following amended paragraph:

Figures 73A-73E:

Intron 1R: Reverse Sequence (SEQ ID NO:121)

Please replace the paragraph on page 18, lines 30 and 31 with
the following amended paragraph:

Figures 75A-75C:

Intron 2F: Forward Sequence (SEQ ID NO:122)

Please replace the paragraph on page 18, lines 33 and 34 with
the following amended paragraph:

Figures 75A-75C:

Intron 2R: Reverse Sequence (SEQ ID NO:123)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 6

Please replace the paragraph on page 18, lines 36 and 37 with the following amended paragraph:

Figures 76A-76B:

Intron 3F: Forward Sequence (SEQ ID NO:124)

Please replace the paragraph on page 19, lines 2 and 3 with the following amended paragraph:

Figures 77A-77B:

Intron 3R: Reverse Sequence (SEQ ID NO:125)

Please replace the paragraph on page 19, lines 5 and 6 with the following amended paragraph:

Intron 4F: Forward Sequence (SEQ ID NO:126)

Please replace the paragraph on page 19, lines 8 and 9 with the following amended paragraph:

Figures 79A-79E:

Intron ~~4RF~~ 4R: Reverse Sequence (SEQ ID NO:127)

Please replace the paragraph on page 22, lines 9-14 with the following amended paragraph:

In the preferred embodiment of this invention, the isolated nucleic sequence is cDNA from human as shown in Figures 47A-47D (SEQ ID NO:1). This human sequence was submitted to GenBank (Los Alamos National Laboratory, Los Alamos, New Mexico) with Accession Number, M99487 and the

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 7

description as PSM, Homo sapiens, 2653 base-pairs.

Please replace the paragraph on page 49, lines 18-28 with the following amended paragraph:

PSMA Antigen Peptide Sequences:

2T17 #5 SLYES (W) TK (SEQ ID. [No.] NO:2)
2T22 #9 (S) YPDGXNLP GG (g) VQR (SEQ ID [No.] NO:3)
2T26 #3 FYDPMFK (SEQ ID [No.] NO:4)
2T27 #4 IYNVIGTL (K) (SEQ ID [No.] NO:5)
2T34 #6 FLYXXTQIPHLAGTEQNFQLAK (SEQ ID [No.] NO:6)
2T35 #2 G/PVILYSDPADYFAPD/GVK (SEQ ID [No.] NOS:7 and 8)
2T38 #1 AFIDPLGLPDRPFYR (SEQ ID [No.] NO:9)
2T46 #8 YAGESFPGIYDALFDIESK (SEQ ID [No.] NO:10)
2T47 #7 TILFAS(W)DAEEFGXX(Q)STE(E)A(e) (SEQ ID [No.] NO:11)

Please replace the paragraph on page 50, lines 16 and 17 with the following amended paragraph:

PSM Primer "A" TT (C or T) - TA (C or T) - GA (C or T) - CCX - ATG - TT (SEQ ID [No.] NO:12)

Please replace the paragraph on page 50, lines 19 and 20 with the following amended paragraph:

PSM Primer "B" AAC - ATX - GG (A or G) - TC (A or G) - TA (A or G) - AA (SEQ ID [No.] NO:13)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 8

Please replace the paragraph on page 50, line 25 with the following amended paragraph:

Peptide 4: IYNVIGTL (K) (SEQ ID [No.] NO:5 6)

Please replace the paragraph on page 50, lines 27 and 28 with the following amended paragraph:

PSM Primer "C" AT (T or C or A) - TA (T or C) - AA (T or C) - GTX - AT (T or C or A) - GG (SEQ ID [No.] NO:14)

Please replace the paragraph on page 50, lines 30 and 31 with the following amended paragraph:

PSM Primer "D" CC (A or T or G) - ATX - AC (G or A) - TT (A or G) - TA (A or G or T) - AT (SEQ ID [No.] NO:15)

Please replace the paragraph on page 50, line 36 with the following paragraph:

Peptide 2: G/PVILYSDPADYFAPD/GVK (SEQ ID [No.] NOS:7-8)

Please replace the paragraph on page 51, lines 1 and 2 with the following amended paragraph:

PSM Primer "E" CCX - GCX - GA (T or C) - TA (T or C) - TT (T or C) - GC (SEQ ID [No.] NO:16)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 9

Please replace the paragraph on page 51, lines 4 and 5 with the following amended paragraph:

PSM Primer "F" GC (G or A) - AA (A or G) - TA (A or G) -
TXC - GCX - GG (SEQ ID [No.] NO:17)

Please replace the paragraph on page 51, lines 12 and 13 with the following amended paragraph:

PSM Primer "I" ACX - GA (A or G) - CA (A or G) - AA (T or
C) - TT (T or C) - CA (A or G) - CT (SEQ ID [No.] NO:18)

Please replace the paragraph on page 51, lines 15 and 16 with the following amended paragraph

PSM Primer "J" AG - (T or C) TG - (A or G) AA - (A or G)
TT - (T or C) - TG (T or C) - TC - XGT (SEQ ID [No.]
NO:19)

Please replace the paragraph on page 51, lines 18 and 19 with the following amended paragraph:

PSM Primer "K" GA (A or G) - CA (A or G) - AA (T or C) -
TT (T or C) CA (A or G) - CT (SEQ ID [No.] NO:20)

Please replace the paragraph on page 51, lines 21 and 22 with the following amended paragraph:

PSM Primer "L" AG - (T or C) TG - (A or G) AA - (A or G)
TT - (T or C) TG - (T or C) TC (SEQ ID [No.] NO:21)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 10

Please replace the paragraph on page 51, lines 28 and 29 with the following amended paragraph:

Peptide 7: **TILFAS (W)DAEEFGXX (q)STE (e) A (E)...** (SEQ ID [No.] NO:11)

Please replace the paragraph on page 51, lines 31 and 32 with the following amended paragraph:

PSM Primer "M" TGG - GA (T or C) - GCX - GA (A or G) - GA (A or G) - TT (C or T) - GG (SEQ ID [No.] NO:22)

Please replace the paragraph on page 51, lines 34 and 35 with the following amended paragraph:

PSM Primer "N" CC - (G or A) AA - (T or C) TC - (T or C) TC - XGC - (A or G) TC - CCA (SEQ ID [No.] NO:23)

Please replace the paragraph on page 52, line 1 with the following amended paragraph:

GA (A or G) - TT (SEQ ID [No.] NO:24)

Please replace the paragraph on page 52, lines 3 and 4 with the following amended paragraph:

PSM Primer "P" AA - (T or C) TC - (T or C) TC - XGC - (A or G) TC - CCA (SEQ ID [No.] NO:25)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 11

Please replace the paragraph on page 55, line 3 with the following amended paragraph:

ACG GAG CAA AAC TTT CAG CTT GCA AAG (SEQ ID [No.] NO:29)

Please replace the paragraph on page 55, line 4 with the following amended paragraph:

T E Q N F Q L A K (SEQ ID [No.] NO:30)

Please replace the paragraph on page 55, lines 15 and 16 with the following amended paragraph:

CTC TTC GGC ATC CCA GCT TGC AAA CAA AAT TGT TCT (SEQ ID [No.] NO:31)

Please replace the paragraph on page 55, lines 20-23 with the following amended paragraph:

AGA ACA ATT TTG TTT GCA AGC TGG GAT GCC AAG GAG (SEQ ID [No.] NO:32)

R T I L F A S W D A E E (SEQ ID [No.] NO:33)

Please replace the paragraph on page 57, line 32 to page 58, line 6 with the following amended paragraph:

Experimental Results

The gene which encodes the 100KD PSM antigen has been identified. The complete cDNA is shown in SEQ ID NO:1. ~~Sequence ID #1~~. Underneath that nucleic acid sequence is the predicted translated amino acid sequence. The total number of the amino acids is 750[,] (SEQ ID [#] NO:128)

[2].

The hydrophilicity of the predicted protein sequence is shown in Figures 16:1-11. Shown in Figures 17A-17C are three peptides with the highest point of hydrophilicity. They are: Asp-Glu-Leu-Lys-Ala-Glu (SEQ ID [No.] NO:34); Asn-Glu-Asp-Gly-Asn-Glu (SEQ ID [No.] NO:35); and Lys-Ser-Pro-Asp-Glu-Gly (SEQ ID [No.] NO:36).

Please replace the paragraph on page 58, lines 8-12 with the following amended paragraph:

By the method of Klein, Kanehisa and DeLisi, a specific membrane - spanning domain is identified. The sequence is from the amino acid #19 to amino acid #44: Ala-Gly-Ala-Leu-Val-Leu-Ala-Gly-Gly-Phe-Phe-Leu-Leu-Gly-Phe-Leu-Phe (SEQ ID [No.] NO:37).

Please replace the paragraph on page 92, line 33 and page 93, line 27 with the following amended paragraph:

Polymerase Chain Reaction: The PSA outer primers used span portions of exons 4 and 5 to yield a 486 bp PCR product and enable differentiation between cDNA and possible contaminating genomic DNA amplification. The upstream primer sequence beginning at nucleotide 494 in PSA cDNA sequence is 5'-TACCCACTGCATCAGGAACA-3' (SEQ ID[.][No.] NO:38) and the downstream primer at nucleotide 960 is 5'-CCTTGAAGCACACCATTACA-3' (SEQ ID[.][No.] NO:39). The PSA inner upstream primer (beginning at nucleotide 559) 5'-ACACAGGCCAGGTATTTCAG-3' (SEQ ID[.][No.] NO:40)

and the downstream primer (at nucleotide 894) 5' GTCCAGCGTCCAGCACACAG-3' (SEQ ID[.][No.] NO:41) yield a 355 bp PCR product. All primers were synthesized by the MSKCC Microchemistry Core Facility. 5µg of total RNA was reverse-transcribed into cDNA in a total volume of 20µl using Superscript reverse transcriptase (Gibco-BRL) according to the manufacturer's ~~manufacturers~~ recommendations. 1µl of this cDNA served as the starting template for the outer primer PCR reaction. The 20µl PCR mix included: 0.5U Taq polymerase (Promega Corp., Madison, WI[.]), Promega reaction buffer, 1.5mM MgCl₂, 200mM dNTPs, and 1.0 M of each primer. This mix was then transferred to a Perkin Elmer 9600 DNA thermal cycler and incubated for 25 cycles. The PCR profile was as follows: 94C x 15 sec., 60C x 15 sec., and 72C for 45 sec. After 25 cycles, samples were placed on ice, and 1µl of this reaction mix served as the template for another round of PCR using the inner primers. The first set of tubes were returned to the thermal cycler for 25 additional cycles. PSM -PCR required the selection of primer pairs that also spanned an intron in order to be certain that cDNA and not genomic DNA were being amplified.

Please replace the paragraph on page 93, line 29 to page 94, line 23 with the following amended paragraph:

The PSM outer primers yield a 946 bp product and the inner primers a 434 bp product. The PSM outer upstream primer used was 5'-ATGGGTGTTTGGTGGTATTGACC-3' (SEQ[.] ID[.][No.] NO:42) (beginning at nucleotide 1404) and the

downstream primer (at nucleotide 2348) was 5' TGCTTGGAGCATAGATGACATGC-3' (SEQ[.] ID[.][No.] NO:43) The PSM inner upstream primer (at nucleotide 1581) was 5'- ACTCCTTCAAGAGCGTGGCG-3' (SEQ[.] ID[.][No.] NO:44) and the downstream primer (at nucleotide 2015) was 5' AACACCATCCCTCCTCGAACC-3' (SEQ[.] ID[.][No.] NO:45). cDNA used was the same as for the PSA assay. The 50l PCR mix included: 1U Taq Polymerase (Promega), 250M dNTPs, 10mM - mercaptoethanol, 2mM MgCl₂, and 5l of a 10x buffer mix containing: 166mM NH₄SO₄, 670mM Tris pH 8.8, and 2mg/ml of acetylated BSA. PCR was carried out in a Perkin Elmer 480 DNA thermal cycler with the following parameters: 94C x 4 minutes for 1 cycle, 94C x 30 sec., 58C x 1 minute, and 72C x 1 minute for 25 cycles, followed by 72C x 10 minutes. Samples were then iced and 2l of this reaction mix was used as the template for another 25 cycles with a new reaction mix containing the inner PSM primers. cDNA quality was verified by performing control reactions using primers derived from -actin yielding a 446 bp PCR product. The upstream primer used was 5'- AGGCCAACCGCGAGAAGATGA-3' (SEQ[.] ID[.][No.] NO:46) (exon 3) and the downstream primer was 5'-ATGTCACACTGGGGAAGC-3' (SEQ[.] ID[.][No.] NO:47) (exon 4). The entire PSA mix and 10l of each PSM reaction mix were run on 1.5-2% agarose gels, stained with ethidium bromide and photographed in an Eagle Eye Video Imaging System (Stratagene, Torrey Pines, CA[.]) Assays were repeated at least 3 times to verify results.

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 15

Please replace the paragraph on page 104, line 26 to page 105, line 1 with the following amended paragraph:

Cloning of PSM promoter. A bacteriophage P1 library of human fibroblast genomic DNA (Genomic Systems, Inc., St. Louis, MI), was screened using a PCR method of Pierce et al. Primers located at the 5' end of PSM cDNA were used: 5'-CTCAAAGGGGCGGATTTC-3' (SEQ ID NO:48) and 5'-CTCTCAATCTCACTAATGCCTC-3' (SEQ ID NO:49). A positive clone, P683, was digested with XhoI restriction enzyme. Southern analysis of the restricted fragments using a DNA probe from the extreme 5' to the Ava-I site of PSM cDNA confirmed that a 3Kb fragment contains the 5' regulatory sequence of the PSM gene. The 3 kb XhoI fragment was subcloned into pKSBluescript vectors and sequenced using the dideoxy method.

Please replace the paragraph on page 107, lines 9-23 with the following amended paragraph:

Polymerase Chain Reaction. Oligonucleotide primers (5'-CTCAAAGGGGCGGATTTC-3' (SEQ ID NO:50) and 5'-AGGCTACTTCACTCAAAG-3') (SEQ ID NO:51), specific for the 5' and 3' ends of PSM cDNA were designed to span the cDNA sequence. The reaction was performed in a 50 µl volume with a final concentration of the following reagents: 16.6 mM NH₄SO₄, 67 mM Tris-HCl pH 8.8m, acetylated BSA 0.2 mg/ml, 2mM MgCl₂, 250 µM dNTPs, 10mM β-mercaptoethanol, and 1 U of rTth polymerase (Perkin Elmer, Norwalk, CT). A total of 25 cycles were completed with the following

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 16

profile: cycle 1, 94°C 4 min.; cycle 2 through 25, 94°C 1 min, 60°C 1 min, 72°C 1 min. The final reaction was extended for 10 min at 72°C. Aliquots of the reaction were electrophoresed on 1% agarose gels in 1X Tris-acetate-EDTA buffer.

Please replace the paragraph on page 119, line 15 to page 120, line 11 with the following amended paragraph:

Polymerase Chain Reaction. The PSA outer primer sequences are nucleotides 494-513 (sense) in exon 4 and nucleotides 960-979 (anti-sense) in exon 5 of the PSA cDNA ~~cDNA~~. These primers yield a 486 bp PCR product from PSA cDNA that can be distinguished from a product synthesized from possible contaminating genomic DNA.

PSA - 494 5'-TAC CCA CTG CAT CAG GAA CA-3' (SEQ ID NO: 38)

PSA - 960 5'-CCT TGA AGC ACA CCA TTA CA-3' (SEQ ID NO: 39)

The PSA inner upstream primer begins at nucleotide 559 and the downstream primer at nucleotide 894 to yield a 355 bp PCR product.

PSA - 559 5'-ACA CAG GCC AGG TAT TTC AG-3' (SEQ ID NO: 40)

PSA - 894 5'-GTC CAG CGT CCA GCA CAC AG-3' (SEQ ID NO: 41)

All primers were synthesized by the MSKCC Microchemistry Core Facility. 5 µl of total RNA was reverse-transcribed into cDNA using random hexamer primers (Gibco-BRL) according to the manufacturer's ~~manufacturers~~ recommendations. 1 l of this CDNA served as the starting

template for the outer primer PCR reaction. The 20 µl PCR mix included: 0.5U Taq polymerase (Promega) Promega reaction buffer, 1.5mM MgCl₂, 200 µM dNTPs, and 1.0 µM of each primer. This mix was then transferred to a Perkin Elmer 9600 DNA thermal cycler and incubated for 25 cycles. The PCR profile was as follows: 94°C x 15 sec., 60°C x 15 sec., and 72°C for 45 sec. After 25 cycles, samples were placed on ice, and 1 µl of this reaction mix served as the template for another 25 cycles using the inner primers. The first set of tubes were returned to the thermal cycler for 25 additional cycles. The PSM outer upstream primer sequences are nucleotides 1368-1390 and the downstream primers are nucleotides 1995-2015, yielding a 67 bp PCR product.

Please replace the paragraph on page 120, line 13 to page 121, line 7 with the following amended paragraph:

PSM - 1368 5'-CAG ATA TGT CAT TCT GGG AGG TC-3' (SEQ ID NO:52)

PSM - 2015 5'-AAC ACC ATC CCT CCT CGA ACC-3' (SEQ ID NO:46)

The PSM inner upstream primer span nucleotides 1689 - 1713 and the downstream primer span nucleotides 1899 - 1923, yielding a 234 bp PCR product.

PSM - 1689 5'-CCT AAC AAA AGA GCT GAA AAG CCC-3' (SEQ ID NO:53)

PSM - 1923 5'-ACT GTG ATA CAG TGG ATA GCC GCT- 3' (SEQ ID NO:54)

2 µl of cDNA was used as the starting DNA template in the

PCR assay. The 50 μ l PCR mix included: 1U Taq polymerase (Boehringer Mannheim), 250 M cNTPS, 10mM β -mercaptoethanol, 2mM $MgCl_2$, and 5 μ l of a 10x buffer mix containing: 166mM NH_4SO_4 , 670mM Tris pH 8.8 and 2mg/ml of acetylated BSA. PCR was carried out in a Perkin Elmer 480 DNA thermal cycler with the following parameters: 94°C x 4 minutes for 1 cycle, 94°C x 30 sec., 58°C x 1 minute, and 72°C x 1 minute for 25 cycles, followed by 72°C x 10 minutes. Samples were then iced and 2.5 μ l of this reaction mix was used as the template for another 25 cycles with a new reaction mix containing the inner PSM primers. cDNA quality was verified by performing control reactions using primers derived from the β -2 microglobulin gene sequence¹⁰ a ubiquitous housekeeping gene. These primers span exons 2-4 and generate a 620 bp PCR product. The sequences for these primers are:

β -2 (exon 2) 5'-AGC AGA GAA TGG AAA GTC AAA-3' (SEQ ID NO:55)

β -2 (exon 4) 5'-TGT TGA TGT TGG ATA AGA GAA-3' (SEQ ID NO:56)

The entire PSA mix and 7-10 μ l of each PSM reaction mix were run on 1.5-2% agarose gels, stained with ethidium bromide and photographed in an Eagle Eye Video Imaging System (Stratagene ~~Statagene~~, Torrey Pines, CA[.]). Assays were repeated at least twice to verify results.

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 19

Please replace the paragraph on page 145, line 4 to page 148,
line 3 with the following amended paragraph:

**GENOMIC ORGANIZATION OF PSM EXON/INTRON JUNCTION
SEQUENCES**

EXON 1 INTRON 1

1F. Strand

CGGCTTCCTCTTCGG (SEQ ID NO:57)

cggcttcctcttcgg taggggggcgcctcgcgag ...tatttttca (SEQ ID
NO.:58)

1R strand ...ataaaaagtCCCACCAA (SEQ ID NO:59)

Exon 2 Intron 2

2F. strand

ACATCAAGAAGTTCT (SEQ ID NO:60)

acatcaagaagttct caagtaagtccatactcgaag (SEQ ID NO:61)

2R. strand ...caagtggtcATTAAATG (SEQ ID NO:62)

Exon 3 Intron 3

3F. strand

GAAGATGGAAATGAG (SEQ ID NO:63)

gaagatggaaatgag gtaaaatataaataaataa... (SEQ ID NO:64)

Exon 4 Intron 4

4F. strand

AAGGAATGCCAGAGG (SEQ ID NO:65)

aaggaatgccagagg taaaaacacagtgcacaaa... (SEQ ID NO:66)

4R. strand ...agagttgTCCCGCTAGAT (SEQ ID NO:67)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 20

Exon 5 Intron 5

5F. strand

CAGAGGAAATAAGGT (SEQ ID NO:68)

CAGAGGAAATAAGGT aggtaaaaattatctctttttt... (SEQ ID NO:69)

...gtgttttctAGGTTAAAAATG (SEQ ID NO:70)

5R. strand ...cacttttgaTCCAATTT (SEQ ID NO:71)

Exon 6 Intron 6

6F. strand

GTTACCCAGCAAATG (SEQ ID NO:72)

gttaccagcaatg gtgaatgatcaatccttgaat... (SEQ ID NO:73)

6R. strand ...aaaaaaagtCTTATACGAATA (SEQ ID NO:74)

Exon 7 Intron 7

7F. strand

ACAGAAGCTCCTAGA (SEQ ID NO:75)

acagaagctcctaga gtaagtttgaagaaaccargg... (SEQ ID NO:76)

7R. strand ...aaacacaggttatcTTTTTACCCA (SEQ ID NO:77)

Exon 8 Intron 8

8F. strand

AAACTTTTCTACACA (SEQ ID NO:78)

aaacttttctacaca gttaagagactatataaatttta... (SEQ ID NO:79)

8R. strand aaacgtaatcaTTTTCAGTTCTAC (SEQ ID NO:80)

Exon 9 Intron 9

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 21

9F. strand

AGCAGTGGAACCAG (SEQ ID NO:81)

agcagtggaaccag gtaaaggaatcgtttgctagca... (SEQ ID NO:82)

...tttctagatAGATATGTCATTC (SEQ ID NO:83)

9R. strand ...aaagaTCTGTCTATACAGTAA (SEQ ID NO:84)

Exon 10 Intron 10

10F. strand

CTGAAAAAGGAAGG (SEQ ID NO:85)

ctgaaaaaggaagg taatacaaacaatatagcaagaa... (SEQ ID NO:86)

Exon 11 Intron 11

11F. strand

TGAGTGGGCAGAGG (SEQ ID NO:87)

Agagg ttagttggtaatTTGctataatata... (SEQ ID NO:88)

Exon 13 Intron 12

12R. strand

GAGTGTAGTTTCCT (SEQ ID NO:89)

Gtagtttcct gaaaataagaaaagaatatagat... (SEQ ID NO:90)

Exon 14 Intron 13

13R. strand

AGGGCTTTTCAGCT (SEQ ID NO:91)

agggcttttcagct acacaaattaaaagaaaaaaag... (SEQ ID NO:92)

Exon 14 Intron 13

14F. strand

GTGGCATGCCCAGG (SEQ ID NO: 93)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 22

gtggcatgcccagg taaataaatgaatgaagtttcca... (SEQ ID NO:94)

Exon 16 Intron 15

15R. strand

AATTGTTTGTTC (SEQ ID NO:95)

aatttgtttgttcc tacagaaaaacaacaaaaca... (SEQ ID
NO:96)

Exon 16 Intron 16

16F. strand

CAGTGTATCATTTG (SEQ ID NO:97)

cagtgtatcatttg gtatgttacccttcctttttcaaatt... (SEQ ID
NO:98)

...tttcagATTCACCTTTTTT (SEQ ID NO: 99)

16R. strand aaagtcTAAGTGAAAA (SEQ ID NO:100)

Exon 17 Intron 17

17F. strand

TTTGACAAAAGCAA (SEQ ID NO:101)

ttttgacaaaagcaa gtatgttctacatatatgtgcatat... (SEQ ID
NO:102)

17R. strand ...aaagagtcGGGTTA (SEQ ID NO:103)

Exon 18 Intron 18

18F. strand

GGCCTTTTTATAGG (SEQ ID NO:104)

ggcctttttatagg taaganaagaaaatatgactcct... (SEQ ID NO:105)

18R. strand ...aatagttgTGTAACCC (SEQ ID NO:106)

Applicants: Ron S. Israeli, et al.
Serial No.: 10/751,346
Filed: January 2, 2004
Page 23

Exon 19 Intron 19

19F. strand

GAATATTATATATA (SEQ ID NO:107)

gaatattatatata gttatgtgagtggtttatatatgtgtgt... (SEQ ID
NO:108)

Notes: F: Forward strand

R: Reverse strand

Please add the Sequence Listing attached hereto as **EXHIBIT B.**